



Living-unrelated donor renal transplantation: an alternative to living-related donor transplantation?

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ABSTRACT

INTRODUCTION An increasing number of living-unrelated, kidney donor transplants are being performed in our unit. We present a comparison of living-unrelated (LURD) and living-related donor (LRD) renal transplant outcomes and analyse influencing factors.

PATIENTS AND METHODS We retrospectively analysed the outcome of all living-donor renal transplants performed at our centre from 1993 to 2004. The parameters studied included patient and graft survival, functioning status of grafts (determined by estimated GFR) at last follow-up and any rejection episodes. Multivariate analysis was performed for recipient and donor age, ethnicity, HLA matching and re-transplants.

RESULTS A total of 322 live donor kidney transplants (LRD, $n = 261$; LURD, $n = 61$) were carried out over this period. Mean recipient age was 28 ± 16 years in the LRD group and 48 ± 12 years in LURD, while mean age of the donors was 43 ± 11 years and 48 ± 10 years, respectively. Caucasians constituted 80% of all the living donors. Amongst LRD, parents were the commonest (58%) donors followed by siblings (35%). In LURD, 80% were spouses. A total of 33 grafts failed, 30 in LRD (11%) and 3 in LURD (5%). Thirteen patients died, 11 (4.2%) in LRD (7 with functioning graft) and 2 (3.3%) in LURD (1 with functioning graft). Acute rejections occurred in 41% recipients in LRD and 35% in LURD ($P = 0.37$). Estimated GFR was lower in LURD than in LRD (49 ± 14 versus 59 ± 29 ml/min/1.73 m²; $P = 0.032$). One- and 3-year patient survival for LRD and LURD was 98.7% and 96.3% and 97.7% and 95%, respectively ($P = 0.75$). One- and 3-year graft survival was equivalent at 94.8% and 92.3% for LRD, and 98.4% and 93.7% for LURD, respectively ($P = 0.18$).

CONCLUSIONS Outcome of LRD and LURD is comparable in terms of patient and graft survival, acute rejection rate and estimated GFR despite differences in demographics, HLA matching and re-transplants of recipients.

KEYWORDS

Living donors – Renal transplantation – Living unrelated donors

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Renal transplantation is an established treatment for end-stage renal disease (ESRD). One of the major factors restricting wider use of this treatment is limited availability of the donor kidneys. Deceased donor source is insufficient to meet the increasing demand. Amongst currently available options, living donors (related and unrelated) constitute a very useful source of the best quality organs with excellent outcome. Superior outcome with living donor transplants compared with cadaveric donor transplants has been widely reported.¹ Therefore, a shift towards living donor transplants is already evident world-wide.² A similar trend has been observed in our unit over the last decade.

The purpose of this study was to compare the outcome of living-related (LRD) and living-unrelated (LURD) donor transplant to see if there were any differences between the two groups in graft survival, patient survival and graft function. We also analysed factors that could have influenced the patient and graft survival.

Patients and Methods

Data were collected from hospital records related to 322 living donor kidney transplants performed in our centre between 1993 and 2004.

Most patients received cyclosporine-based immunosuppression. In LRD, 69% ($n = 180$) of patients received azathioprine and 31% ($n = 81$) mycophenolate mofetil (MMF). A total of 24% ($n = 63$) received Tacrolimus either as primary therapy or switch over. Basiliximab induction was used in 29% ($n = 76$). In LURD, respective figures were 65% ($n = 40$), 35% ($n = 21$), 26% ($n = 16$) and 32% ($n = 20$). Mean follow-up was 45 months.

Outcome measures studied were graft and patient survival, estimated GFR at the follow-up and acute rejections. GFR was estimated using the Nankivell Modification of Diet in Renal Disease (MDRD) equation in adults and the Schwartz formula in patients less than 19 years of age.^{5,4} The diagnosis of acute rejection was based on histology. Graft and patient survival were estimated by the Kaplan–Meier method and compared by log-rank test. Patients dying with functional grafts were censored as failed grafts. Multivariate analysis was done by the Cox proportional hazard model to see whether recipient and donor age, ethnicity, HLA matching and re-transplants influenced the outcome. Variables such as cold ischaemia time that were unlikely to be different in the two groups were not included in the analysis. Nominal variables were analysed by Chi-square test and numeric variables by Mann–Whitney U-test.

Results

A total of 261 living-related donor (LRD) and 61 living-unrelated donor (LURD) transplants were performed during the period. Baseline characteristics of the patients are shown in Table 1. Thirty-three grafts failed, 30 in LRD (11%) and 3 in LURD (5%). A total of 13 patients died; 11 of these had LRD transplants (4.7%). Seven patients (54%)

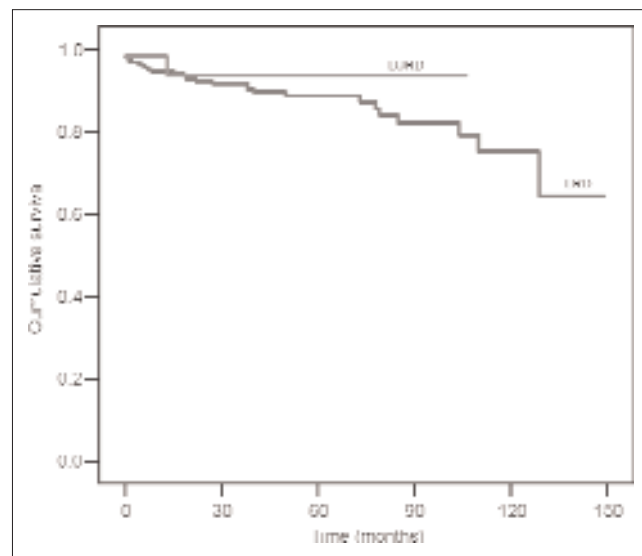


Figure 1 Graft survival in LRD and LURD.

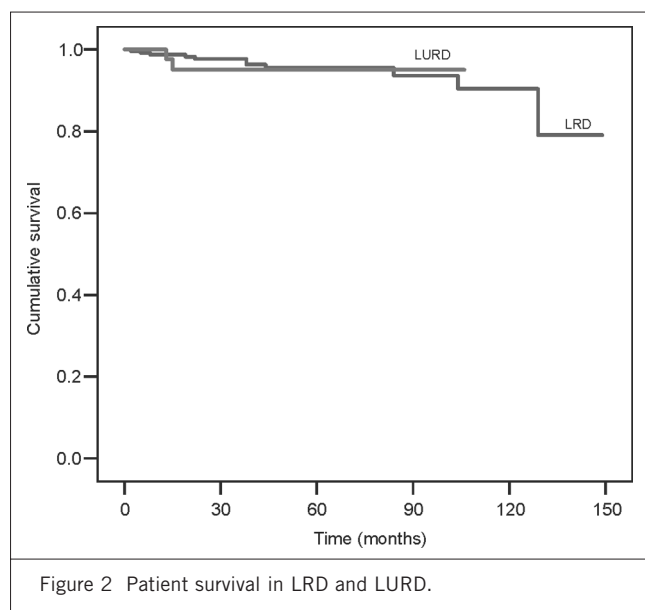
had functioning grafts at the time of their death. Two patients in the LURD group (3.3%) died, one with a functioning graft. Acute rejections occurred in 41% in LRD and 35% in LURD. The difference was not statistically significant ($P = 0.37$). Estimated GFR was lower in LURD than in LRD (49 ± 14 versus 59 ± 29 ml/min/1.73 m²; $P = 0.032$).

Thirty grafts in the LRD group failed because of acute rejection (36%; $n = 11$), chronic rejection (4%; $n = 1$), vascular or ureteric complications (20%; $n = 6$), recurrent disease (3%; $n = 1$), death of recipient (24%; $n = 7$) and 13% ($n = 4$) due to unknown causes. In the LURD group, there were three graft failures due to acute and chronic rejection (one each) and one of unknown cause.

Table 1 Patients' baseline characteristics

| Characteristic | LRD | LURD |
|------------------------------|---|--|
| Mean recipient age (years) | 28 ± 16 | 48 ± 12 |
| Recipient sex (M:F) | 1:1.5 | 1:3 |
| Mean donor age (years) | 43 ± 11 | 48 ± 10 |
| Donor sex (M:F) | 1:15 | 1:2 |
| Ethnicity | Caucasian 79% Others ^a 21% | Caucasian 96% Others 4% |
| Relationships | Parents 58% ($n = 143$) Siblings 35% ($n = 88$) Others ^b 7% (18) | Spouses 80% ($n = 49$) Others ^c 20% ($n = 12$) |
| HLA mismatches (mean and SD) | 2.0 ± 1.2 | 3.9 ± 1.2 |
| Re-transplants | 10% ($n = 20$) | 3% ($n = 2$) |

^aAsians, Afro-Caribbean, Orientals; ^bSecond-degree relatives; ^cStep-relatives, friends.



In the LRD group, the deaths ($n = 11$) were due to acute myocardial infarction ($n = 2$), cerebrovascular accident ($n = 2$), graft failure ($n = 1$), tuberculosis ($n = 1$) and unknown reasons ($n = 5$). Two patients who died in the LURD group were as a result of road traffic accident) and an unknown cause.

One- and 3-year graft survival (Fig. 1) estimates were 94.8% and 92.3% for LRD, and 98.4% and 93.7% for LURD, respectively ($P = 0.18$). One- and 3-year patient survival (Fig. 2) estimates for LRD and LURD were 98.7% and 96.3% and 97.7% and 95%, respectively ($P = 0.75$). Recipient age, donor age, HLA matching, and re-transplants did not affect the outcome.

Discussion

Living-donor renal transplantation is becoming increasingly popular because of better quality organs and excellent outcomes. There has been a general increase in living-donor transplantation world-wide. We have observed a similar trend in our unit over the past decade. During the first 3 years of the study period, 8% ($n = 25$) of all transplants were living-donor transplants amongst which 2% ($n = 1$) were LURD. In the last 3 years, the figures have increased to 44% ($n = 136$) and 26% ($n = 35$), respectively. Since the introduction of laparoscopic nephrectomy, the living donation rate has been reported to be significantly increased.⁵ The adoption of this technique is also a reason for the increasing trend of living donation at our centre in recent years.

The majority of patients in the LRD group were offspring who received kidneys from their parents, which explains the significantly lower mean age of recipients in this group

($P < 0.01$). Younger age is regarded as a risk factor for higher rejection rate due to the stronger immunological milieu.⁶ In our series, although the rejection rates in the LRD group were relatively higher, it did not reach statistical significance. Likewise, graft survival was not significantly affected by recipient age.

In the LURD group, the majority of donors were patients' spouses. Gjertson *et al.*⁷ compared spouse and other genetically unrelated transplants and found no difference in graft survival. We could not make such comparison due to the small number of cases in the two subgroups. HLA mismatches are known to have an important bearing on outcome of transplants as shown by the recent registry data analysis.^{2,8} However, many recent single-centre studies have reported similar graft survival rates with LRD and LURD in spite of greater HLA mismatches in LURD.^{9,10} In our study, although LURD had significantly higher HLA mismatches than LRD ($P < 0.001$), HLA mismatch did not have any adverse effect on the outcome. HLA mismatches might have contributed to some early rejections observed in the LURD group. Further, while HLA mismatches are reported to effect long-term graft survival, our study with a mean follow-up of 45 months is focused on short-term results.¹¹

Ethnicity is known to influence outcome in the transplant recipients.^{12,13} Our LRD population was ethnically more diverse than the LURD group. However, numbers in ethnic subgroups were too small to make a valid comparison.

Rejection rates vary widely in recent series comparing LRD and LURD due to discrepancies in rejection criteria and differences in immunosuppression protocols. Matas *et al.*¹ studied acute rejections greater than 6 months post-transplant and reported rejection rates of 8.6% in LURD and 2.6% in LRD. Fuller *et al.*¹⁴ reported 1-year acute rejection rates of 30% in LURD and 18.5% in LRD. Voiculescu *et al.*¹⁸ found much higher rejection rates – 54.2% in LURD and 52.2% in LRD; these authors used antibody induction very selectively. Campbell *et al.*¹⁵ reported 44% acute rejections in living donors versus 28% in cadaveric donors with the use of more frequent antibody induction in the latter (20% versus 8%).

GFR estimation by the MDRD or Schwartz formulae, though not exact, allows better estimation of kidney function than conventional serum creatinine levels. Although the estimated GFR was lower in LURD than LRD, the difference was not statistically significant ($P < 0.1$).

Our survival curves are valid only in the short term due to the limited period of follow-up. However, 1- and 3-year graft and patient survival is similar to many of the recently reported single-centre series.^{14,16}

Despite reports of excellent outcome in unrelated donor transplants, this donor source remains under-utilised.

Donation by spouses is also low amongst the potentially available donors.¹¹ Ethical issues and potential commercialism are the main obstacles to genetically unrelated donor transplants, the latter particularly in non-industrialised countries. It is crucial to strike a balance so that patients could benefit from this invaluable organ source while avoiding donor exploitation by stringent scrutiny of any unrelated living donors.¹⁷

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